SYNOPSIS

DETERMINATION OF SELECTED TRACE ELEMENTS IN HUMAN AUTOPSY TISSUES COLLECTED FROM AJMER REGION

अजमेर क्षेत्र में मानव शव–विच्छेदन द्वारा प्राप्त उत्तकों में सूक्ष्म तत्त्वों का परीक्षण

SUBMITTED TO

MAHARSHI DAYANAND SARASWATI UNIVERSIY
AJMER (RAJASTHAN)

For Ph.D in Forensic Chemistry

Name of Scholar
Kavita Kumari
Lecturer
SPC Govt. College
Ajmer (Rajasthan)

Name of the Supervisor
Dr. R.K. Tak
Lecturer
SPC Govt. College
Ajmer (Rajasthan)

Appendix-IV-A

MAHARSHI DAYANAND SARASWATI UNIVERSITY, AJMER

Outline (Synopsis) of Proposed Research Work
(Reference Ord. 124.11)

1 **Name of Scholar (In English) :** KAVITA KUMARI
(In Hindi) : कविता कुमारी

2 **Title of the Research work**
In English Determination of selected trace elements in human autopsy tissues collected from Ajmer region

In Hindi अजमेर क्षेत्र में मानव शव–विच्छेदन द्वारा प्राप्त उत्तकों में सूक्ष्म तत्त्वों का परीक्षण

3. **Location:**

a. **Institution/Department where the work is to be done:**
- Dept. of Chemistry, SPC Government College, Ajmer (Rajasthan)
- Dept. of Environmental Sciences, MDS University, Ajmer (Rajasthan)
- Forensic Medicine Department, JLN Medical College & Hospital, Ajmer (Rajasthan)

b. **Geographical area of Investigation, if any.** :- Ajmer Region

c. **4. Introduction, Importance of proposed investigation, objective.** :-Annexure- I (a,b,c)

d. **Review (Work already done on the subject of proposed Research Study.)** :- Annexure-II

e. **Research Gaps identified in the proposed field of investigation. (Based on the review):** :- Annexure-III

f. **Major Hypothesis, if any** :- Annexure-IV

g. **Research Methodology.** :- Annexure-V

h. **List of Reference Cited:** :- Annexure-VI

26.4.16

Signature of the Candidate with Date

Outline Approved

26.4.16

Name and Signature of Supervisor with date and seal

Lecturer in Chemistry
SPC Govt. College, AJMER

APPENDIX - VI

MAHARSHI DAYANAND SARASWATI UNIVERSITY, AJMER

Certificate by Supervisor

Certified that:

1. I am willing to guide the research work of Mrs. Kavita Kumari on the above subject if she is registered for Ph.D.

2. To the best of my knowledge, the subject selected has not studied and is not being studied so far in any University.

3. The subject is of sufficient scope to keep the candidate engaged for two years.

4. The subject will lead to a valuable contribution. I have seen and approved the outline of proposed research work submitted by the candidate.

5. I have 2...Research candidates registered under my supervision and the serial number of this candidate whose application is being forwarded for registration is .5..(give the serial number).

6. The candidate is not in a close relation (the term of close relation is defined in the examination ordinance of the University).

26.4.16

Signature of the Supervisor with date

Lecturer in Geography
Govt. College, AJMER

Certified that the available facilities will be extended to Mrs. Kavita Kumari for research work if she is registered for Ph.D.

26/4/16

Signature of the Principal of the institute with date

26.4.16

Signature of the Head of the Dept. with date

INTRODUCTION

In this modern era of urbanization, the persisting environment with respect to industrialization, changing climate, food habits, life style etc, have strongly affected the human health. The impact of environment in which we live is strongly reflected upon the human body, its physiology and metabolic activity. Trace elements like Fe, Mn, Zn, Co, Cu, Mo, Se, I plays vital role and have been recognized well for their role in growth and development, in the past few decades clinical interest in studying the level of trace elements in human body and their impact on health have sought attention for study. Recently Graves *et al.,*[1] suggested that global differences exist in body composition, ethnicity and age. Variation may be noted for trace elements with respect to age, gender, growth, body composition, genetics, alcohol abuse, infections, diseases, dietary factors. Hence, on a global basis, trace element requirements can vary according to geographical location, food preparation and processing, food accessibility, cultural practices (geophagia) and pollution,

Therefore, the study of trace elements not only helps to understand the physiological role, but they also provide insight into the dynamism happening within the human body with respect to the environment over location and time. The daily human activity needs air, water and food for survival, but these essential life components are sourced from the existing environment, which might have changed with course of time, and even it may get deteriorated due to pollutions and heavy metals also. A continuous exposure to a polluted environment can alter the human body metabolism and may also affect the elemental concentration at cellular level. These trace elements including heavy metals may cause serious disorders or diseases due to deficiency or toxicity. Study from fluids like blood and urine samples reflects elemental status circulating at the time of sampling, which may sometime be not correlated with degree of exposure. Hair analyses indicate past exposure, but are not strong reflective of body burden but tissue biopsies for elemental analysis can help in the diagnosis of diseases related to contaminated environment exposure (Bush *et. al.,*)[2].

IMPORTANCE

There is need to understand and acquire fundamental data related to trace elements in human body. Study with respect to human samples from various geographical locations is needed as location is strongly associated to environment and life style. Henceforth, a study of trace elements in major organs like kidney, liver, lungs, spleen etc., and comparative analysis of these estimates among the population with respect to age, sex, food habits etc can help in assessing the status of elements in respective human population of the region and will also help is correlating any deficiency or toxicity symptoms of trace element on human body.

Autopsy sampling of tissue is preferably more accessible for wider range of organs compared to living human subjects. A detailed study of elemental composition in various organs can altogether lead to detection of status of element in normal humans over a region or location and further association can also be established with certain disease states based on human sample history. In past, Tipton and Cook[3] surveyed extensively population of United States of America and found that chromium depletion is widespread in their country. Likewise regional population should be studied from time to time to understand the dynamic changes happening in humans with respect to environment.

Ajmer population is exposed to air pollution caused by motor vehicles, industries and other urbanization factors, whereas rural population resides in less air polluted climate. The food habits of rural and urban population also vary. In past, case studies done by Mehra and Juneja[4] and other groups on hair and nail samples of Ajmer population on trace/toxic metals reports high variation for the trace metals. Hence, it suggests that variation exists in Ajmer population and a detailed study of trace elements at organ level will add more to the understanding with respect to Ajmer population. Further correlation studies with other important factors like age, sex, adaptability conditions of rural or urban area, past disease history etc., can be very much helpful in understanding the present status and importance of trace elements in human health with respect to Ajmer condition in general.

Annexure-I (c)

OBJECTIVES

The present research will be undertaken with the following objectives:

- To estimate the content of trace elements in autopsy sample of human kidney
- To estimate the content of trace elements in autopsy samples of human liver
- To estimate the content of trace elements in autopsy samples of human lung
- To collect data from the family of the death person with the help of a questionnaire to develop background data for association studies
- To perform association studies among the trace element content and parameters recorded for each person with the help of questionnaire as per objective 3

REVIEW OF WORK ALREADY DONE ON THE SUBJECT OF PROPOSED RESEARCH STUDY

Graves *et. al.,*[1] presented the global perspective of trace elements and mentioned that global differences exist in body composition, ethnicity and age[6]. They suggested that requirements of trace elements can vary according to age, gender, growth, body composition, genetics, pregnancy, lactation, wound healing and burns, alcohol abuse, infections, and diseases. Additionally, interactions may occur with dietary factors, geographical location, food preparation and processing, food accessibility, cultural practices (geophagia) and pollution.

Bush *et. al.,*[2] studied human autopsy samples for concentrations of five essential elements and six potentially toxic elements in seven organs from 30 human subjects[2]. There was no more than a 10-fold difference in the tissue concentration of the elements studied among the organs, except for the concentration of Fe in liver, and Ca and Mg in bone.

Tipton and Cook[3] estimated values of 24 trace elements in 29 different tissues of 150 adult victims of instantaneous death in population of United States of America

Mehra and Juneja[4] studied the hairs Ajmer population exposed to trace/toxic metals at workplace, they found significant correlation between skin diseases, chest pain, hypertension, mental stress, liver problem, indigestion, diabetes, tuberculosis, breathing problem with trace element content[13]. Hairs were used as biomarkers for assessing metal body burden.

Gil and Hernández[5] suggested that human biomonitoring has become an important tool for the assessment of internal doses of metallic and metalloid elements[5]. These elements are of great significance because of their toxic properties and wide distribution in environmental compartments. Although blood and urine are the most used and accepted matrices for human biomonitoring but other non-conventional samples may have practical advantages and would provide additional information on health risk.

Hongda *et. al.,*[6] undertook studies to provide reference values for relevant parameters of Chinese Reference Man[7]. Eighteen kinds of major organ or tissue samples, including muscle, rib, liver, and so on, were obtained from autopsies of 68 healthy adult men living in four areas of China with different dietary patterns (Hebei, Shanxi, Sichuan, Jiangxi or Jiangsu provinces, including Shanghai City) who had just encountered sudden deaths

Yaman[7] studied the roles of metals in the development and inhibition of cancer, because of their essential and toxic effects on human health[20]. Question of whether trace metal concentrations in tissues are increased or decreased in cancerous patients in comparison with noncancerous patients has not been answered yet, due to the fact that the data known in this field is rare and have contradictory results. Although Zn and Cu concentrations in serum and tissues of cancerous patients have been extensively studied, the precise role of these metals in carcinogenesis is not clearly understood.

Katoh *et. al.,*[8] in order to elucidate the distribution of elements in organs from healthy Japanese, did preliminary examination for quantitative determination of multielements in nine organs autopsied (brain, heart, kidney, liver, lung, muscle, pancreas, spleen, and thyroid). The values obtained for each element could be considered to be representative as "normal values" and "ranges" in organs from healthy Japanese males; the essential elements Br, Cl, Co, Cu, Fe, K, Mn, Na, Rb, Se, and Zn were not affected by external environmental factors or by racial difference; (3) renal and hepatic Cd levels were very high in several cases and the accumulation has still been in progress in the Japanese, whereas the contaminant elements are low in each organ except for lung.

Falnoga *et. al.,*[9] studied total Hg and Se concentrations in autopsy samples of retired Idrija mercury mine workers, Idrija residents living in a Hg-contaminated environment, and a control group with no known Hg exposure from the environment[4]. In selected samples we also checked the presence of MeHg. The highest Hg concentrations were found in endocrine glands and kidney cortex, regardless of the group. Cd concentrations were the highest, particularly in kidney cortex and thyroids (μg/g), but no relationship between Cd and Se concentration was evident at the tissue level. Regarding the results in the control group, it is debatable which element is the more hazardous for the general population as concerns neurotoxicity.

Iyengar[10] reevaluated using recent analytical data, the total body content of several trace elements for the 70 kg Reference Man[8]. With respect to dietary intakes, in contrast to the earlier estimates intakes of trace elements were found to be decreased by factors of 2 for Cu, 2–5 for Cr, 5–10 for Cd, Hg and Pb, and >10 for Ag, As, Co, Li, Sb and V.

Tiran *el. at.,*[11] investigated selenium and cadmium concentrations in 60 autopsy tissue samples in Styria, a moderately industrialized region in Austria that has a low selenium supply. In summary, the data revealed very low tissue selenium concentrations and low cadmium burdens for the Styrian population that was not exposed occupationally.

Yoshinaga *et. al.*,[12] studied elemental concentrations of internal organs (cerebrum, cerebellum, heart, spleen, liver and kidney) of Japanese[21]. Sixty-one elements were determined simultaneously, and concentrations of some trace elements in human organs, on which information are scarcely available in the literature, were obtained. Unacceptable values were obtained for some elements, such as Ti, Sc or Ge, probably due to polyatomic molecular interference.

Muramatsu and Parr[13] analysed autopsy samples of hair, liver and kidney cortex from 30 Swedish subjects (Caucasian) for Ag, Co, Cr, Hg, Sb, Se and Zinc[14]. The following elements were observed to have higher concentrations in hair than in liver and kidney cortex: Ag, (Co), Cr and Hg (on a dry weight basis).

Iyengar and Wolttlez[14] suggested reference values for the concentrations of As, Cd, Co, Cr, Cu, Fe, Hg, Mn, Mo, Pb, Se, and Zn in whole blood, blood serum, urine, milk, liver, and hair from adult human subjects[4]. For F, I, and Ni, it was not possible to evaluate reference interval for all the specimes mentioned above.

Subramanian and Meranger[15] performed multi-element determination of major, minor and trace elements in human liver and kidney specimens[10]. A total of 20 elements in about 40 autopsy samples of human kidney (cortex and medulla) and liver taken from Canadian adults living in the Great Lakes Region of Ontario were determined.

Carpenter[16] digested human liver and kidney tissue by the proteolytic enzyme to get suitable solutions for direct determinations of Cd, Cu, Pb and Tl[13]. Good precision and accuracy were demonstrated. Normal concentrations of Cd and Cu were determined in these tissues.

Locke[17] used flame atomic-absorption spectrometric method for the determination of Ca, Mg, Zn, Fe, Cu, Mn, Rb and Cd in human liver tissue[12].

Vouri *et. al.*,[18] studied autopsy specimens of aorta, heart, kidney, liver, lung, pancreas and skeletal muscle of 86 accident victims[19]. According to the results the Finnish population does not differ, on the average, from other populations with respect to tissue copper concentrations.

Soman *et. al.*,[19] studied major and trace elements content in human tissues collected from Bombay, India[16]. Data on elemental content in twenty tissues/organs collected from twenty cases of instantaneous accidental death of normal adults were presented.

Annexure-III

RESEARCH GAPS IDENTIFIED IN THE PROPOSED FIELD OF INVESTIGATION (BASED ON THE REVIEW)

Trace elements role in human health have been recognized well, recent advances and review of research work on these aspects suggest that trace element can vary according to age, gender, growth, body composition, genetics, pregnancy, lactation, wound healing and burns, alcohol abuse, infections, and diseases. Interactions may occur with dietary factors, geographical location, food preparation and processing, food accessibility, cultural practices (geophagia) and pollution. Biomonitoring of trace elements is essential with time to know the status and its impact on human health (Gill and Hernandez)[5]

Ajmer population has been studied in past for the variation in trace/toxic metals in hairs and nails as biopsy sample (Mehra and Junega)[4], they correlated the trace/toxic element with various disease observed in the population under study. Which reflects that variation for trace element content exist in the region due to environmental factors, but no studies have been done on Ajmer population for trace element content status in human organs. Human organs have been studied in many cases for the elemental composition across the world and emphasis has been laid on its correlation with the human health. Taking the advantage of the existing variation available in the population of Ajmer for elemental composition, it's an opportunity to study in detail the content of these trace elements in important organs like kidney, liver and lungs. The study will provide valuable information for the trace elements and its correlation with other factors.

Annexure-IV

MAJOR HYPOTHESIS, IF ANY

The population residing in and around Ajmer are living in a dynamic environment affected by urbanization day by day, moreover variable life styles also rests due to urban and rural culture of living. Altogether these factors strongly influence the human body, clinical studies on hairs in past (Mehra and Juneja)[4] on Ajmer population have reported variation of trace elements and their effect on human health.

Henceforth these past studies suggest that variation may exist in Ajmer population with respect to trace element in organs. Therefore, proposed study is advanced on organ level to know the status of trace element content in major human organs like kidney, liver and lungs which can help us to understand the human health status of the region. These estimates can be correlated with various parameters which are part of human activity to assess the role of environment on human health.

Annexure-V

RESEARCH METHODOLOGY

- Human organ samples (Autopsy) will be collected with the help of Forensic medicine Department, JLN College & Hospital, Ajmer (Rajasthan) as per availability and accessibility of the samples on random basis
- Selected trace elements in kidney, liver and lung tissues will be estimated by assessing the acid digested sample in Atomic Absorption Spectrophotometer available in the Department of Environmental Sciences, MDS University, Ajmer (Rajasthan) following standard protocols (IAEA)[20]
- Questionnaires with respect to data on each sample will be filled with the help of family members of the sample for performing correlation studies on trace element content and other environmental factors
- Data analysis will be performed using standard statistical procedures using suitable software like (SPSS, Microsoft excel etc.)

Annexure-VI

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26.4.16

Signature of the Candidate with Date